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# FUNGAL HEALTH EFFECTS UPDATE

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# Objectives

- Review the most current literature on the health effects of molds in indoor environments
  - Epidemiology
  - Mechanisms
- Discuss data needs and research efforts
- Consider implications for management of indoor environmental problems
- Consider implications for clinical evaluation/ management

# Background

- More than 70,000 species of fungi
- Human responses
  - Immunologic
    - Allergy – asthma, sinusitis
    - Organic toxic dust syndrome (ODTS), HP
  - Infectious – immune compromise
- Many produce some toxigenic compounds (mycotoxins)

# Allergic Disorders and Building Fungal Contamination

- Question:  What do we know about the relationship between molds and fungi and the development of asthma?
- Barnes et al., 2001
  - Dust samples from 47 children's homes measured for allergens including *Alternaria alternata, Cladosporium herbarum, Aspergillus fumigatus* (as well as cat, dog, mite, cockroach, other common antigens); compared with clinical diagnoses of allergies, asthma
  - Asthmatic children had significantly higher concentrations of *Alternaria*, as well as dust mite

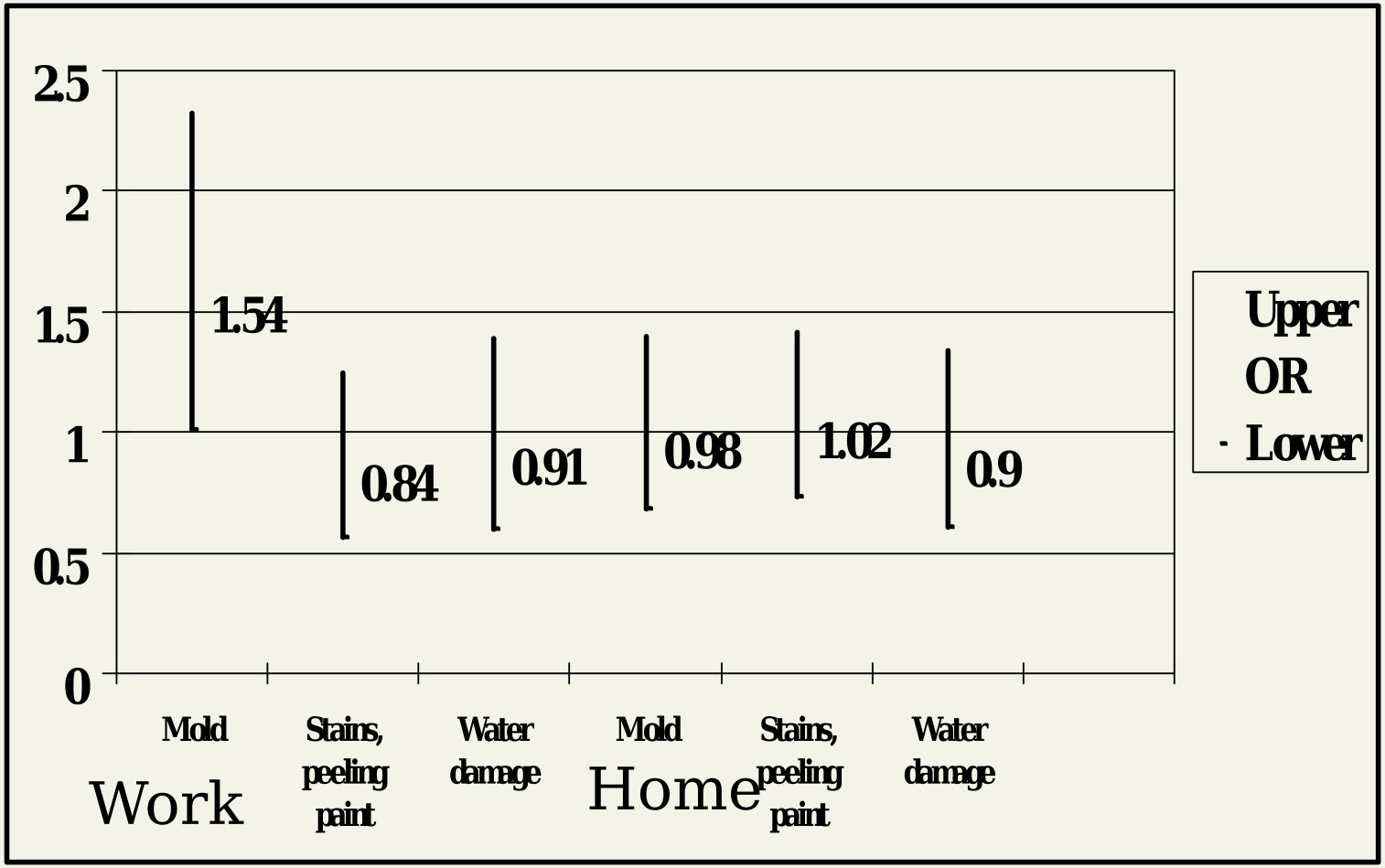
# Epidemiology of Allergic Sensitivity to Fungi

- Barnes et al. (2002) – measured IgE- and IgG-reactivity to *S. chartarum* in 132 anonymous serum samples – 49.2% were IgG positive, and 9.4% were IgE positive [Kansas City].
- Beeh et al. (2001) – 306 randomly selected subjects at an inner city pulmonary practice. No association of severe asthma with *Alternaria* sensitivity [Frankfurt].
- Other studies indicate newborns may be at increased risk of sensitization, particularly with very high exposures

# Dampness, Mold, Adult-Onset Asthma

- Jaakkola et al. 2002. – recruited all new onset adult asthma cases (N=521) and controls (N=932) from 1997 – 2000.
- Exposure – self-reported water damage, visible mold, mold odor (plus confounders)

# Adjusted Odds of Self-Reported Exposures and New-Onset Asthma




Adapted from Jaakkola et al. 2002

# *Stachybotrys* and Human Disease

- Occurrence
  - Outdoors – rarely found in air samples; can be cultered from soil, plants (hay, straw, grains), and animal hair (dog, cat, cow, donkey, monkeys)
  - Indoors – associated with water damage, building surfaces containing cellulose
  - Human disease – *Fusarium* linked to alimentary toxic aleukia (ATA), a mycotoxin-related GI disease in Russians around WWII

# Satratoxins

- Macrocyclic trichothecenes
- Enzymes – B-glucanase, 1,3-endoglucanase, farnesyl-protein transferase
- Sesquiterpenes
- Stachybocins
- Stachybotramide
- Stachybotrin C
- Staplabin and its analogs

# Case Reports

- Trout et al. (2001) – 48 year old with dry cough, fever & dyspnea after invasively assessing mold damage in his hotel
- Elevated total IgE; IgG to *Thermoactinomyces vulgaris*, no specific IgG or IgE to *Stachybotrys*
- NIOSH looked at serum of 6 exposed, 2 unexposed hotel workers, found increased IgG to roridin-albumin (hapten of a macrocyclic trichothecene) in one exposed, one unexposed worker. No increased IgM in any worker.

# Mechanisms of Injury

- Vesper and Vesper (2002) – Stachylasin (a hemolysin) injected into earthworms, died after hemorrhage and aneurysm formation
- Model of possible mechanism implicated in infant pulmonary hemorrhage

# Pathway From Source to Disease

**Environmental factors**
**Aerosol distribution**

**Exposure**

**<u>Biological Response</u>**
**Early biological effects**
**Clinical response**

**<u>Host factors</u>**
**Genetic**
**Metabolic**
**Other**

# Research Needs and Opportunities

- Source – need better understanding of fungal growth, toxin production
- Transmission/distribution – how are fungi transmitted in the environment?
- Exposure – what is the relationship between ambient concentration and internal exposure and dose? Biological markers of exposure not well characterized
- Biological effects – need better understanding of allergic, non-allergic effects, susceptibility factors

# Secondary Effects of Fungal Exposure

- Direct health effects lead to secondary effects
  - Quality of life
  - “Presenteeism” – effects on work
- Kessler et al. (2001) – allergic rhinitis salary-equivalent monthly cost estimated to be equivalent to $156.27/employee, or $7.7 billion annually in lost productivity

# Issues in Clinical Management

- Presentation
- Diagnostic studies
- Building evaluation
- Medical management and return to work
- Worker protection during remediation

# Presentation

- History
- Exacerbating, mitigating factors
- Onset – risk factors?
- What do we know about new-onset allergies and relationship to exposures?

# Use of Specific Diagnostic Testing

- Skin Prick Testing
  - Limited utility in building-related cases?
- RAST
- Peak Flow Meters
- Methacholine challenge
- Imaging
- Neurocognitive
- Immunologic testing
  - Lessons from MCS

# Building Evaluation

- Visual inspection
- Sampling
  - Bulk vs. air vs. MVOC
  - PCR?

# Management

- Medical management
- Issues in removal
- Issues in return to work
  - Role of “clearance”
    - Background rates
    - Visual inspection
- Prevention
  - Role for UV?
    - Levetin et al:  UV decreases fungi in air handling unit fiberglass insulation
    - Menzies et al: UV irradiation of drip pans and cooling coils (double-blind crossover trial) resulted in reductions in “work-related” symptoms (including respiratory, mucosal, and musculoskeletal)

# Worker Protection During Remediation

- Workers need respiratory, dermal protection
- Controversy regarding appropriate level of protection

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